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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,144	03/25/2004	Robert Costa	03-284-E	7397

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EXAMINER	
HALVORSON, MARK	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
06/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,144	COSTA ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3, 8-10 and 50-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *54-56* is/are allowed.

6)☒ Claim(s) *1-3,8-10 and 51-53* is/are rejected.

7)☒ Claim(s) *50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/27/08;4/3/08;6/2/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Claims 1-3, 8-10 and 50-56 are pending and are under examination.

35 USC § 112 1st paragraph rejection maintained

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-3, 8-10 and new claims 51-53 for failing to comply with the enablement requirement is maintained.

Claims 1-3, 8-10 and 51-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting proliferation of a tumor cell comprising the step of inhibiting FoxM1B activity in the tumor cell by contacting the cell with a p19ARF protein fragment *in vitro*, and a method of inhibiting proliferation of a liver tumor cell comprising the step of inhibiting FoxM1B activity in the tumor cell by contacting the cell with a p19ARF protein fragment *in vivo* does not reasonably provide enablement for a method of inhibiting proliferation of any tumor cell comprising the step of inhibiting FoxM1B activity in the tumor cell by contacting the cell with a p19ARF protein fragment *in vivo*. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make o ruse the invention commensurate in scope with these claims.

Applicants argue that Office has not established a prima facie case of non-enablement and that the success in treating liver tumors *in vivo* using an animal model is sufficient evidence that the p19ARF 26-44 peptide will be successful in treating any type of tumor, Applicants argue that the specification is not required to contain evidence of actual reduction to practice, much less actual reduction to practice in every tumor model.

Applicants further argue that the Declaration of Dr. I-Ching Wang demonstrates that FoxMIB is expressed in a variety of tumor cells, not just liver tumor cells, and that the pl9ARF peptide may have broad therapeutic benefits in treating different types of cancers. Applicants argue that one of skill in the art would have been able to, at the time of the invention, use the peptide to treat different types of tumors without undue experimentation.

Applicants arguments have been considered but are not persuasive. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." As previously stated the art of anticancer drug discovery is an unpredictable art. As such more guidance is required than other areas. Although *in vivo* data is not required it is one factor to consider and is especially relevant in highly unpredictable areas. Furthermore, the guidance in the specification and the in vitro working examples in the specification and the post-filing *in vivo* data in the Declaration by Dr Wang are not commensurate in scope with the present claims. The claims are

drawn to a method of inhibiting proliferation of a tumor cell whereas the working examples in the specification demonstrate that the protein fragment of SEQ ID NO:10 inhibited the colony formation of a human osteoblastoma cell. Given the significant differences between the various types cancer and the unpredictability of treating cancer one of skill in the art could not predictably treat any type of cancer with the protein fragment of SEQ ID NO:10.

Applicants have previously submitted a Declaration by Dr Wang and state that the post-filing date *in vivo* data supports enablement of the specification. The Declaration shows that the protein fragment of SEQ ID NO:10 injected intraperitoneally into tumor-bearing mice, penetrated into liver cells *in vivo* and altered Foxml cellular localization *in vivo*. The Declaration also shows that the protein fragment of SEQ IDO:10 inhibited hepatocellular tumor proliferation *in vivo*. Applicants have submitted a second Declaration of Dr Wang and copies of research article which indicate that FoxM1B is expressed in many proliferating tumor cell lines and primary tumors. The Declaration of Dr Wang also states that the p19ARF26-44 peptide inhibits tumor progression in osteosarcoma cells and hepatocarcinoma cell lines as well as inhibited the Fox M1B-dependent transactivation in the lung adenocarcinoma cell line A549. These data has been considered but are not persuasive. The document must present a showing of enablement which is commensurate in scope with the claims or at least as much of the claims as have been objected to *In re Armbruster*, 158 USPQ 152. The examples present in the Declaration must be sufficient to show enablement for the entire scope of the claimed subject matter. The Declaration demonstrates that the protein fragment of SEQ ID:10 inhibited hepatocellular tumor proliferation *in vivo* but the claims are drawn to a method of inhibiting proliferation of any type of tumor. Applicants are not required to demonstrate an actual reduction to practice in every tumor model. However, Applicants have only demonstrated an actual reduction to practice in one tumor model. The reduction of practice for one tumor model and the demonstration that the protein fragment of SEQ ID NO:10 has an effect on a few tumor cell lines *in vitro* is not sufficient to enable the full scope of the present claims. Given the disclosure

in the specification, and the Declarations by Dr Wang, one of skill in the art could not predictably treat any type of cancer with the protein fragment of SEQ ID NO:10.

Therefore, in view of the breadth of the claims, lack of guidance in the specification, the narrow scope of the working examples in the specification and the Declaration and the state of the art it would require undue experimentation to practice the invention as broadly claimed.

Summary

Claims 1-3, 8-10 and 51-53 stand rejected.

Claim 50 is objected to for being dependent on a rejected claim.

Claims 54-56 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson
Patent Examiner
571-272-6539

/MISOOK YU/
Primary Examiner, Art Unit 1642